Imaging Biomarkers Predict Neurologic Recovery after Thoracolumbar Spinal Cord Injury

Undergraduate Research Thesis

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Introduction

Spinal cord injuries (SCI), defined as "damage to any part of the spinal cord or nerves at the end of the spinal canal," range widely in severity and mechanism. [1] In the United States, the prevalence (the number of people currently living with spinal cord injuries) is estimated at 250,000 cases. The annual incidence (the rate of cases per person-time) is estimated at 40 cases/ million people/year, which equates to approximately 11,000 new cases each year. [2, 3] These metrics do not uniformly affect the entire population with non-Hispanic whites being primarily affected and mortality ranging from 3.1 to 17.5 per million people. [4] The most common modes of injury are motor vehicle accidents and falls. [5]

The region of the spine affected and the mechanism of injury can greatly influence the injury severity. Patients with SCI incur great cost for their chronic treatment needs, with the average patient in 2017 spending $74,509 dollars per year directly on care. [5] Patients with more severe injuries incur higher costs for treatment, as well as increased social and economic ramifications. Spinal cord injuries translate into occupational disadvantage, as from 1 to 20 years post injury, only 12.4% to 34% of SCI patients are employed, respectively. Since SCI can confer great social and economic consequences, our ability to prognosticate neurological and functional recovery is critical to patient counseling and to planning of resource allocation. Further, proper classification of SCI severity can help clinicians provide tailored treatment plans to limit further damage and improve neurologic outcomes.

Clinicians divide SCI into two components: primary and secondary injury. The primary injury stems from the mechanical impact, and can include variable degrees of contusion, compression, deceleration, shear, distraction, and laceration. Fortunately, irreversible laceration injuries are highly uncommon in human populations because of the amount of force needed to

transect the cord. The secondary injury occurs in the hours, days, and weeks following the primary injury. Secondary injury mechanisms include parallel processes of early necrosis, ischemia, excitotoxicity, and free radical formation. [8] These processes contribute to further cell death and exacerbate the severity of the initial injury. As such, these secondary injuries are the target of current therapeutic interventions.

Much of current SCI research revolves around investigating measures to better prognosticate neurologic recovery with regard to sensory and motor abilities. In this paper, I will investigate the relative ability of various neuroimaging biomarkers to serve as surrogate measures of injury severity and of neurologic recovery in the chronic recovery phase following SCI. The relevant admission magnetic resonance imaging (MRI) study parameters are defined on page 7 of this text. [6] Maximum Canal Compromise (MCC), Maximum Spinal Cord Compression (MSCC), Intramedullary Lesion (IML) length, extent of hyperintensity within the spinal cord on axial views (Brain and Spinal Injury Center; BASIC score), as well as the combined axial and sagittal (CASS) score each may independently predict the likelihood of neurological improvement. Specifically, the ASIA impairment scale (AIS) grade is an ordinal classification system used to assess the severity of SCI (Appendix 1). The grades range from A through E, with A being the most severe injury with no sensory or motor preservation below the level of injury, even in the sacral region. The sensory score is generated using light touch and pin prick testing at dermatomes associated with specific regions of the spinal cord. The motor score is assessed using muscle force testing. These metrics are combined to define both the level and severity of injury.

Previous studies have shown differential rates of AIS grade conversion following cervical SCI when admission AIS grade is stratified by either IML, BASIC, or CASS scores (Figure 1).

[7] Similar statistical testing will be employed here to assess the potential significance of these admission findings in the context of thoracolumbar SCI.

Due to the traumatic nature of SCI, patients often present with comorbidities that make initial neurologic evaluations difficult. Due to the anatomical location of the thoracic spine, thoracic SCI often result from high velocity and high impact mechanisms that makes these patient cohorts even more heterogeneous. The use of neuroimaging biomarkers as surrogate measures for injury severity may also help to further stratify patients in clinical trials to assess for potential therapeutic benefit.

Methods

Research Questions

- What is the ability of various admission imaging parameters in predicting neurologic recovery for patients with thoracolumbar SCI?
- Can these biomarkers be used to better stratify thoracolumbar SCI patient populations to decrease heterogeneity in clinical trial cohorts?

Study Population

A total of 551 patient medical records tagged for thoracic SCI were reviewed. From this population, a total of 26 patients fit the inclusion criteria, and were included in this analysis (Table 1). Males were disproportionately represented, accounting for 87% of the injuries. The mean age of the cohort was 40.9 ± 14.9 years, and 11 patients had a score of at least 1 on the Charlson Comorbidity Index (CCI). The CCI is a measurement that predicts the 10-year survival of a patient. As patients present with greater comorbidities, their chance of 10-year survival

decreases. Motor vehicle accidents represented the most common primary injury mechanism, followed by fall from height, 54.8% and 19.2% of injuries, respectively. 73.1% of patients had an Injury Severity Score (ISS) of > 25. The ISS is a measure of the number of systems involved in a trauma patient. Typically, patients with a score of greater than 25 are considered to be severe traumas. 53.8% of patients were classified as AIS grade A upon admission. 14 of the 26 injuries were to the level of T7-T12, but the cohort also had representation of SCI from T1-T6 and L1-L2. Only 30.8% of patients received steroid therapy following their injuries, while 96.2% underwent surgery. Of these surgeries, 53.8% were completed within 24 hours of the initial injury. One patient passed during the initial hospital admission period, and 2 passed during the 1-year follow-up period. Of note, the patient who passed during initial hospitalization also did not undergo surgery.

Study Design

Institutional Review Board approval was obtained and followed throughout the duration of the study. This study was conducted using retrospective analysis. This study design allows for a good estimate of risk, and a clear temporal relationship between exposure (thoracolumbar SCI) and outcomes (neurologic severity and AIS grade conversion). This study design also allows investigators to investigate more than one outcome. However, retrospective studies are potentially hampered by loss-to-follow up as well as potential different modes of data collection across institutions. Data was drawn from the IHIS Electronic Medical Record System using ICD-9 codes associated with thoracic SCI.

Data Collection

Data were collected from 551 patient medical record numbers (MRNs) tagged with ICD-9 codes associated with thoracic SCI. All patients evaluated for thoracic SCI at The Ohio State University Wexner Medical Center including at The Brain and Spine Hospital and Dodd Rehabilitation Center from 2005-2017 were screened. The patients were analyzed with regard to the following inclusion and exclusion criteria (Figure 2).

Inclusion/ Exclusion Criteria

Patients who sustained SCI outside of the thoracolumbar spinal levels or no SCI at all were excluded. Patients who suffered non-traumatic SCI from tumor compression, infection, or osteoarthritis were also excluded. Those who incurred open SCI such as from gunshot wounds or stabbings were also excluded, as the associated transection of the cord leaves no capacity for axonal regeneration. Additionally, patients had to be admitted directly to the Brain and Spine Hospital or Dodd Rehabilitation Center, or transferred from an outside hospital with full documentation of course of treatment and associated imaging. Pre-operative imaging was paramount to assessing the level and extent of injury, as well as identifying hemorrhage or edema. Images were assessed from both sagittal and axial MRI views. Patients who had incomplete data or who were lost-to-follow up were also excluded. As such, the inclusion criteria were as follows: (1) 18 years of age or older; (2) sustained traumatic SCI to the thoracolumbar spine; (3) admitted directly to Ohio State University Wexner Medical Center, or transferred with full documentation of care; (4) presence of admission MRI; (5) availability of one-year follow-up data. The presence of admission imaging was of paramount importance, as

the MRI parameters were used to prognosticate neurologic severity and AIS grade conversion, both at 6 and 12 months.

Study Parameters

- Maximum canal compromise (MCC) and maximum spinal cord compression (MSCC) were used to evaluate canal stenosis and cord compression, respectively. These measures are continuous variables calculated by measuring the diameter of the canal or cord above, at, and below the level of injury on T2-weighted MRI views.
- Intramedullary lesion (IML) length was used to evaluate intrinsic cord signal change within the mid-sagittal cross section of the spinal cord. IML length is a continuous variable that measures the length of the hyperintense signal in the spinal cord on T2 weighted MRI views.
- The BASIC score was used to evaluate intrinsic cord signal change within the spinal cord from an axial cross section. The BASIC score is an ordinal variable that measures the hyperintense foci confined to the grey matter, extending to the white matter, or across the entire transverse section of the axial spinal cord, which correspond to BASIC levels 1, 2, 3, respectively. A BASIC grade 4 corresponds to a grade 3 hyperintensity with the addition of hypointense foci consistent with bleeding within the cord.
- The Combined Axial and Sagittal Score (CASS) was derived to assess the potential importance of axial and sagittal intrinsic cord signal changes when considered together. IML length was converted into an ordinal variable of categories 0-4 and then summed with the BASIC score to ultimately form an 8-point scale.

Statistical Methods

The statistical analyses for this study were conducted using SPSS with a reference significance value of ≤ 0.05. Categorical variables were analyzed with Chi-square tests, and Fisher's Exact test when expected counts were low (Table 3). These categorical variables are presented as the number of subjects and relative frequencies. The ability of the MRI variables to prognosticate neurological severity (that is AIS A or B versus C or D injuries) and AIS grade conversion was assessed by generating receiver operating characteristic (ROC) curve analysis and expressed as area under the curve (AUC) values (Table 4). Continuous variables are presented as the mean and standard deviation or median, when appropriate.

Results

MRI Findings

Thoracic spine MRI studies were performed on admission in 26 patients (Table 2). The mean midsagittal diameter of the spinal canal at the level of injury was 10 ± 2.5 mm, which lead to a mean MCC of 47.3 ± 17.0. MCC was converted from a continuous variable to 3 distinct ordinal categories. 7 (26.9%), 14 (53.8%), and 5 (19.2%) of patients had MCC values of <25, 25-50, or >50, respectively. The mean midsagittal diameter of the spinal cord at the level of injury was 5.1 ± 1.5 mm, which lead to a mean MSCC of 12.1 ± 22.6. MSCC was converted from a continuous variable to 2 distinct ordinal categories. 4 (16.7%) and 20 (83.3%) of patients had MSCC values of <0 or ≥0, respectively.

Intrinsic cord signal changes along the sagittal plane were classified using IML length. The mean rostrocaudal length of intramedullary signal change was 32.1 ± 19.9 mm. IML length was converted from a continuous variable to 5 distinct ordinal categories. 4 (16.0%), 2 (8.0%), 4

(16.0%). 4 (16.0%), 12 (48.0%) of patients had IML lengths of ≤10, 10.1-20. 20.1-30, 30.1-40 and >40, respectively. Intrinsic cord signal changes along the axial plane were classified using the BASIC score. One patient (4.2%) had no signal abnormality (BASIC score 0). Three patients (12.5%) had signal abnormality confined to the grey matter (BASIC score 1). Nine patients (37.5%) had signal abnormality that extended into the white matter (BASIC score 2). Four patients (16.7%) had signal abnormality that involved the entire transverse section of the spinal cord (BASIC score 3). Seven patients (29.2%) had grade 3 injuries plus hypointense foci consistent with hemorrhage (BASIC score 4). The CASS was computed using both the IML category (0-4) and BASIC score (0-4). Five (20.0%), 7 (28.0%), and 13 (52.0%) patients had CASS of ≤ 3, 4-5, ≥ 6, respectively.

Clinical Variables and Outcomes

Clinical variables were analyzed using univariate chi-square testing to assess neurological severity on admission and at one year, and AIS grade conversion at one year (Table 3). Neurological severity was quantified using a binary system, with AIS grade A/B corresponding to a severe injury and AIS grade C/D corresponding to a non-severe injury. These binary values were then quantified as the proportion of subjects in each clinical category. AIS grade conversion was similarly transformed into a binary variable, differentiating between conversion of at least one AIS grade and no conversion. This binary was again quantified as the proportion of subjects in each clinical category.

Age (≤30/ >30 years) was not significantly associated with neurological severity on admission or at one year, or with respect to AIS conversion at one year (p = 0.21, 0.41, 0.58, respectively). Sex was not significantly associated with neurological severity on admission or at

one year, or AIS conversion at one year (p = 0.29, 0.48, 0.37, respectively). CCI was not significantly associated with neurological severity on admission or at one year, or AIS conversion at one year (p = 0.53, 0.76, 0.35, respectively). BMI (≤30/ >30 kg/m^2) was not significantly associated with neurological severity on admission (p = 0.24), but was significantly associated with neurological severity at 1 year and AIS conversion at 1 year (p = 0.01 and <0.01, respectively). Injury mechanism was not significantly associated with neurological severity on admission or at one year, or AIS conversion at one year (p = 0.71, 0.36, 0.41, respectively). ISS (≤25/ >25 years) was not significantly associated with neurological severity on admission or at one year, or AIS conversion at one year (p = 0.42, 0.801, 0.45, respectively). The presence of a concomitant spinal fracture (with / without) was not significantly associated with neurological severity or AIS conversion at one year (p = 0.42 and p = 0.35, respectively). In agreement with the literature, the administration of steroids (with / without) was not significantly associated with neurological severity on admission or at one year, or with AIS conversion at one year (p = 0.95, 0.54, 0.35, respectively). Time from injury to decompression (≤24 / >24 hours) was not significantly associated with neurological severity on admission (p = 0.32), but was significantly associated with neurological severity and AIS conversion at 1 year (p = 0.05 and 0.02, respectively).

MRI Variables and Outcomes

MRI variables MCC, MSCC, IML, BASIC, and CASS were individually assessed using AUC analysis to predict neurological severity and AIS conversion (Table 4). MCC does not show any ability to predict neurologic severity at either 6 or 12 months (AUC 0.33 and 0.33, respectively). MCC also fails to predict AIS grade conversion at either 6 or 12 months (AUC

0.28 and 0.28, respectively). MSCC shows fair ability to predict neurologic severity at 6 or 12 months (AUC, 0.74 and 0.74, respectively). MSCC shows poor ability to predict AIS grade conversion at 6 or 12 months (AUC 0.69 and 0.69, respectively). IML length is an excellent predictor of neurologic severity at both 6 and 12 months (AUC 0.96 and 0.96, respectively). IML length is also an excellent predictor of AIS grade conversion at both 6 and 12 months (AUC 0.93 and 0.93, respectively). The BASIC score is also a reliable predictor of neurologic severity at both 6 and 12 months (AUC 0.89 and 0.89, respectively) as well as AIS grade conversion at both 6 and 12 months (AUC 0.88 and 0.88, respectively). Finally, CASS is an excellent predictor of neurologic severity at both 6 and 12 months (AUC 0.96 and 0.96, respectively) as well as AIS grade conversion at both 6 and 12 months (AUC 0.94 and 0.94, respectively). Subsequent studies will use a combinatorial approach in attempts to increase the predictive value of these measures.

Discussion

All current medical and surgical intervention for SCI management, including ICU care, is aimed at preventing further injury. Several factors contribute to the current lack of neuroprotective and neuroregenerative interventions in human SCI patients. The heterogeneity of SCI in humans coupled with variable rates of spontaneous neurologic recovery, estimated at between 5-25% even in so-called complete AIS A patients, confounds the analysis of the potential therapeutic benefit of novel interventions. Additionally, because of the nature of traumatic SCI, the initial neurologic evaluation often proves to be difficult. Patients often present with altered mental status due to various causes ranging from inebriation to concomitant traumatic brain injuries. Patients also may present with multisystem injuries or spinal shock,

which may further cloud the neurologic evaluation. Spinal shock is a poorly understood phenomenon that results in the temporary suppression of reflex activity below the level of neurologic injury. [12] This phenomenon manifests differently between patients, and often lasts up to 72 hours after injury. Additionally, when evaluating the dermatomes associated with the thoracic spinal cord, poor inter and intra-rater variability is noted. Since the dermatomes for this region of the spine comprise a large area of skin between the nipple and umbilicus, reliable and consistent determination of the injury level often proves difficult. The combination of the aforementioned factors makes initial neurologic evaluation difficult and imprecise. As such, the validation of quantitative biomarkers to assess severity and prognosticate neurological recovery after thoracolumbar SCI would confer advantages in both the clinical and research fields. Improved prognostication would help clinicians better counsel patients with regard to their expected recovery. This counseling is especially important in SCI patients because of the lifelong associated social and economic burdens. In the realm of clinical research, improved prognosticative testing would also allow for more rational clinical trial design with improved patient stratification. Researchers could then better assess the efficacy of neuroprotective and neuroregenerative interventions in thoracolumbar SCI patients.

Thoracic spinal cord injuries represent a particularly heterogeneous cohort, and the injuries can be highly severe and variable. First, since the thoracic spine is nested not only within the rib cage but under soft tissues, a high-impact, high-velocity mechanism is necessary to damage the cord. Second, the thoracic spinal cord sits in a watershed of vascularization, where it receives less blood flow relative to the levels above and below. The narrowing of the canal at the thoracic level has also been implicated in the heterogeneous nature of the injuries. Lastly, patients who sustain injuries above the T6 level have the potential to enter neurogenic shock

subsequent to the significant loss of sympathetic innervation. Neurogenic shock can result in complications like bradycardia and low blood pressure. [13] These complications can further increase the heterogeneous nature of thoracic SCI patient cohorts. The aforementioned variables help to explain why distinct anatomical regions within the thoracic spine show differential rates of neurologic recovery. [9]

This study has allowed for novel insight into the potential of biomarkers to assess the capacity for neurologic recovery after thoracolumbar SCI. We identified associations between clinical factors such as BMI and time to surgery with respect to neurological severity and AIS grade conversion at 1 year (Table 3). The potential role of obesity in neural recovery is not well understood despite numerous studies examining this relationship in pre-clinical SCI models. [14] Conflicting data has emerged in human SCI populations suggesting either a protective or detrimental influence of obesity. [11] A larger sample of thoracolumbar SCI patients is needed to allow for more definitive conclusions regarding the role of obesity in neurologic recovery. Similarly, while the current pre-clinical literature favors early decompression after SCI, supportive data in humans remains scarce that earlier decompression leads to improved neurologic outcomes. [15]

This study found that IML length and CASS were excellent predictors of neurological severity and AIS grade, both at 6 months and 1 year after thoracic SCI (Table 4). The study also showed that the BASIC score is another potential strong predictor of neurological severity and AIS grade conversion. These results are contrary to the findings in cervical SCI patients, where the axial-based BASIC score was more predictive than the sagittal-based IML length. [7] The slightly lower predictive ability of the axial biomarker in this study could have been due to the relatively poorer image quality of the thoracic spinal cord surrounded by the thoracic cavity and

soft tissues. As such, further research with larger patient samples will be needed to more reliably assess the potential differences in predictive ability between sagittal and axial biomarkers following thoracolumbar spinal cord injury.

Conclusions

This study showed that canal stenosis, cord compression, and intrinsic cord signal changes can be measured within a thoracolumbar SCI patient sample. Further, the intrinsic cord signal parameters showed better predictive ability for neurologic severity and AIS grade conversion as compared to measures of stenosis and compression, at both 6 months and 1 year after thoracic SCI. Interestingly, the sagittal-based parameter (IML length) may be a better prognosticator of neurologic severity and AIS grade conversion as compared to the axial-based parameter (BASIC score) after thoracolumbar SCI. Future studies should ideally apply a combinatorial approach to improve the predictive ability of these metrics potentially integrating clinical measures along with these admission imaging parameters. The predictive ability of these measures can be applied to better counsel patients and improve stratification in interventional studies.

References

[1] Spinal cord injury. (2017, December 19). Retrieved from https://www.mayoclinic.org/diseases-conditions/spinal-cord-injury/symptoms-causes/syc-20377890

[2] Richards JS, Go BK, Rutt RD, Lazarus PB. The national spinal cord injury collaborative database. In: Stover SL, DeLisa JA, Whiteneck GG, editors. Spinal cord injury: clinical outcomes from the model systems. Gaithersburg: Aspen; 1995. p 10-20.

[3] Stephan, K., Huber, S., Häberle, S., Kanz, K., Bühren, V., van Griensven, M., et al. (2015). *Spinal cord injury—incidence, prognosis, and outcome: An analysis of the TraumaRegister DGU*doi://doi.org/10.1016/j.spinee.2015.04.041

[4] Jia, X., Kowalski, R. G., Sciubba, D. M., & Geocadin, R. G. (2011). Critical Care of Traumatic Spinal Cord Injury. *Journal of Intensive Care Medicine,28*(1), 12-23. doi:10.1177/0885066611403270

[5] National Spinal Cord Injury Statistical Center, Facts and Figures at a Glance. Birmingham, AL: University of Alabama at Birmingham, 2018.

[6] Cohen-Adad J. Microstructural imaging in the spinal cord and validation strategies. Neuroimage 2018. doi:10.1016/j.neuroimage.2018.04.009.

[7] Kukreja, S., Schwab, J., & Farhadi, F. (2016). 168 Impact of Initial Clinical and Imaging Parameters on Long-Term Neurological Outcomes in Acute Traumatic Cervical Spinal Cord Injury. *Neurosurgery,63*, 167. doi:10.1227/01.neu.0000489737.31599.5b

[8] Rowland, J. W., Hawryluk, G. W., Kwon, B., & Fehlings, M. G. (2008). Current status of acute spinal cord injury pathophysiology and emerging therapies: Promise on the horizon. *Neurosurgical Focus,25*(5). doi:10.3171/foc.2008.25.11.e2

[9] Harrop, J. S., Naroji, S., Maltenfort, M. G., Ratliff, J. K., Tjoumakaris, S. I., Frank, B., Vaccaro, A. R. (2011). Neurologic Improvement After Thoracic, Thoracolumbar, and Lumbar Spinal Cord (Conus Medullaris) Injuries. *Spine,36*(1), 21-25. doi:10.1097/brs.0b013e3181fd6b36

[10] Talbott, J. F., Whetstone, W. D., Readdy, W. J., Ferguson, A. R., Bresnahan, J. C., Saigal, R., Dhall, S. S. (2015). The Brain and Spinal Injury Center score: A novel, simple, and reproducible method for assessing the severity of acute cervical spinal cord injury with axial T2-weighted MRI findings. *Journal of Neurosurgery: Spine,23*(4), 495-504. doi:10.3171/2015.1. spine141033

[11] Blackmer, Jeff, and Shawn Marshall. "Obesity and Spinal Cord Injury: an Observational Study." *Spinal Cord*, vol. 35, no. 4, 1997, pp. 245–247., doi:10.1038/sj.sc.3100392.

[12] Silver, J. R. (2005). Spinal shock revisited: A four-phase model. *Spinal Cord,43*(7), 450-450. doi:10.1038/sj.sc.3101739

[13] Guly, H., Bouamra, O., & Lecky, F. (2008). The incidence of neurogenic shock in patients with isolated spinal cord injury in the emergency department. *Resuscitation,76*(1), 57-62. doi:10.1016/j.resuscitation.2007.06.008

[14] Gordon, T. (2009). The role of neurotrophic factors in nerve regeneration. *Neurosurgical Focus,26*(2). doi:10.3171/foc.2009.26.2.e3

[15] Tecle, N. E., Dahdaleh, N. S., & Hitchon, P. W. (2016). Timing of Surgery in Spinal Cord Injury. *Spine,41*(16). doi:10.1097/brs.0000000000001517

TABLE 1 – CHARACTERISTICS OF PATIENTS (N=26) ADMITTED WITH THORACOLUMBAR TSCIS

	n	%
Demographics		
Sex (male/female))	23/3	87.0/13.0
Age (mean, yrs)	40.9 ± 14.9	
Comorbidities (CCI ≥ 1)	11	42.3
Injury mechanism		
MVA	14	54.8
Fall from height	5	19.2
Sports injury	2	7.7
Mechanical fall	0	0
OHT	5	19.2
ISS		
≤25	19	73.1
>25	7	26.9
AIS grade (admission)		
A	14	53.8
B	2	7.7
C	6	23.1
D	4	15.4
Injury Level		
T1-T6	9	34.6
T7-T12	14	53.8
L1-L2	3	11.5
Use of steroid	8	30.8
Surgery		
Decompression	23	
Fusion	2	
No surgery	1	
Injury to decompression time (≤24 hours)		
≤24 hours	14	53.8
>24 hours	12	46.2
Deaths at initial admission	1	3.4
Deaths at 1 year follow-up	2	7.7

Abbreviations: tSCI – traumatic spinal cord injury; MVA – Motor vehicle accident; OHT –Other high-energy trauma; ISS – Injury severity score; AIS – ASIA Impairment Scale; ASIA – American Spinal Injury Association; Delayed surgery – surgery performed during a subsequent admission.

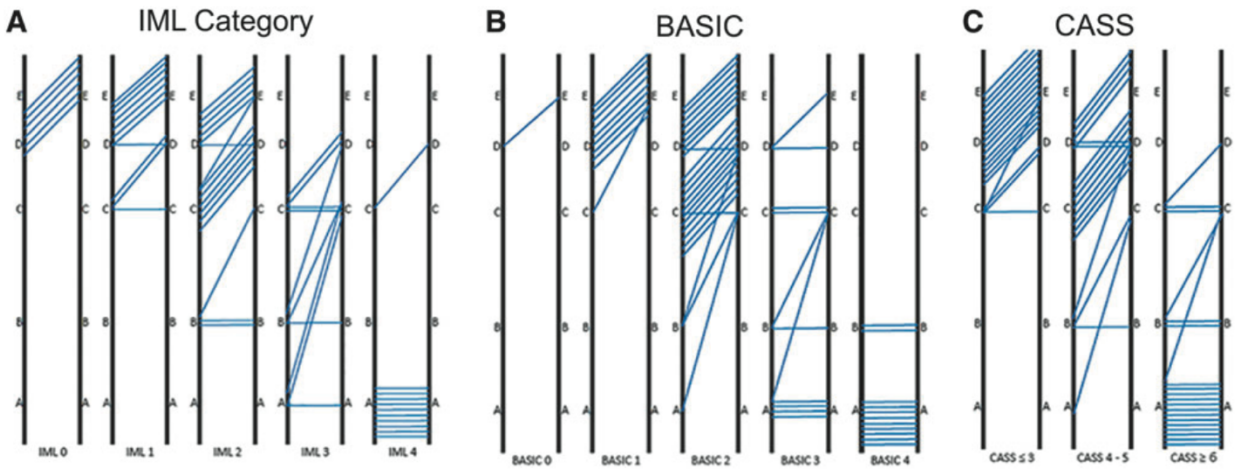


FIGURE 1: CERVICAL SPINAL CORD INJURY PATIENTS SHOW DIFFERENTIAL RATES OF AIS GRADE CONVERSION AT 1 YEAR WHEN STRATIFIED BY IML, BASIC, AND CASS PARAMETERS

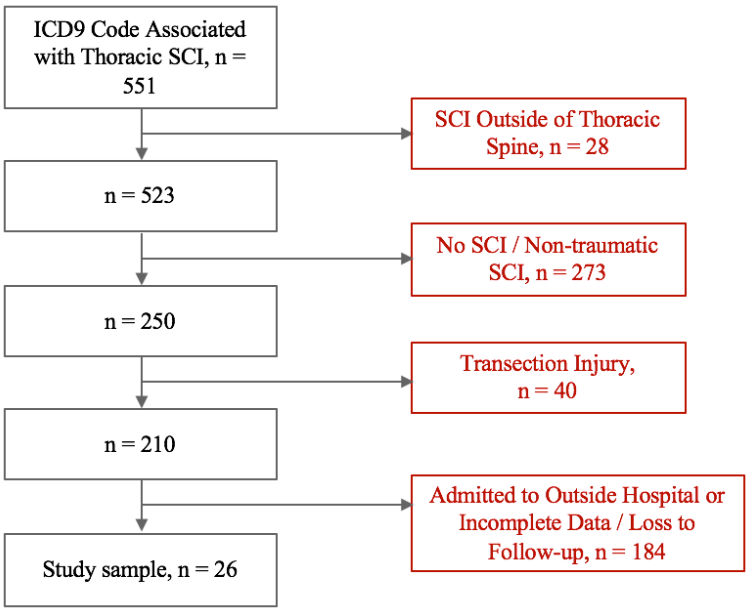


FIGURE 2: APPLICATION OF EXCLUSION CRITERIA

TABLE 2: STUDY PARAMETERS AND VALUES IN THIS STUDY (N=26)

Parameter	Definition (Mean value)	Value (n,%)
Di (mm)	Midsagittal diameter of the spinal canal at injury site (10 ± 2.5)	
Da (mm)	Midsagittal diameter of the spinal canal above injury site (14.9 ± 1.4)	
Db (mm)	Midsagittal diameter of the spinal canal below injury site (14.6 ± 1.6)	
di (mm)	Anteroposterior diameter of the spinal cord at injury site (5.1 ± 1.5)	
da (mm)	Anteroposterior diameter of the spinal cord above injury site (7.0 ± 1.5)	
db (mm)	Anteroposterior diameter of the spinal cord below injury site (6.9 ± 1.4)	
MCC (%)		
MCC <25	[(Da + Db)/2 – Di] / (Da + Db)/2 × 100 (47.3 ± 17.0)	7 (26.9)
MCC 25-50		14 (53.8)
MCC >50		5 (19.2)
MSCC (%)* n=24		
MSCC <0	[(da + db)/2 – di] / (da + db)/2 × 100 (12.1 ± 22.6)	4 (16.7)
MSCC ≥0		20 (83.3)
Length of intramedullary lesion (IML, mm) n=25		
IML ≤10		4 (16.0)
IML 10.1-20	Rostrocaudal length of intramedullary signal changes (32.1 ± 19.9)	2 (8.0)
IML 20.1-30		4 (16.0)
IML 30.1-40		4 (16.0)
IML >40		12 (48.0)
BASIC score n=24		
0	No signal changes	1 (4.2)
1	Signal change confined to central gray matter	3 (12.5)
2	Signal changes extend beyond gray matter to involve white matter	9 (37.5)
3	Signal changes involving entire transverse extent of spinal cord	4 (16.7)
4	Grade 3 plus T2 hypointense foci of macrohemorrhages	7 (29.2)
CASS		
≤ 3	BASIC score (0-4) + longitudinal IML category (0-4)	5 (20.0)
4-5		7 (28.0)
≥ 6		13 (52.0)

Abbreviations: MCC – Maximum canal compromise; MSCC – Maximum spinal cord compression; IML – Intramedullary lesion; BASIC – The Brain and Spinal Injury Center; CASS –Combined axial and sagittal score.

TABLE 3: IMPACT OF CLINICAL FACTORS ON OUTCOMES IN A UNIVARIATE ANALYSIS

Variable	Neurological Severity on Admission (%)	P-value	Neurological Severity at 1 year (%)	P-value	AIS Conversion at 1 year (%)	P-value
Age (≤30/ >30 years)	83.3/55.0	0.21	66.7/46.7	0.41	33.3/46.7	0.58
Sex (Male/Female)	65.2/33.3	0.29	55.6/33.3	0.48	38.9/66.7	0.37
CCI (0/≥1)	66.7/54.5	0.53	50.0/57.1	0.76	50.0/28.6	0.35
BMI ((≤30/ >30)	68.4/42.9	0.24	68.8/0.0	0.01	25.0/100.0	<0.01
Injury mechanism		0.712		0.36		0.41
MVA	57.1		46.2		46.2	
Fall from height	60.0		40.0		60.0	
Sports injury	100.0		100.0		0.0	
Mechanical fall	0.0		0.0		0.0	
OHT	60.0		100.0		0.0	
ISS (≤25/>25)	69.2/53.8	0.42	50.0/55.6	0.801	50.0/33.3	0.45
Spinal fracture (with/without)	60.0/100	0.42	52.4/	-	57.1/35.7	0.35
ASIA grade (admission)				0.00		0.00
A			100.0		0.0	
B			0.0		100.0	
C			0.0		100.0	
D			0.0		100.0	
Use of steroid (with/without)	62.5/61.1	0.95	42.9/57.1	0.54	57.1/35.7	0.35
Injury to decompression time		0.32		0.05		0.02
≤24 hours	50.0		30.0		70.0	
>24 hours	72.7		72.7		18.2	

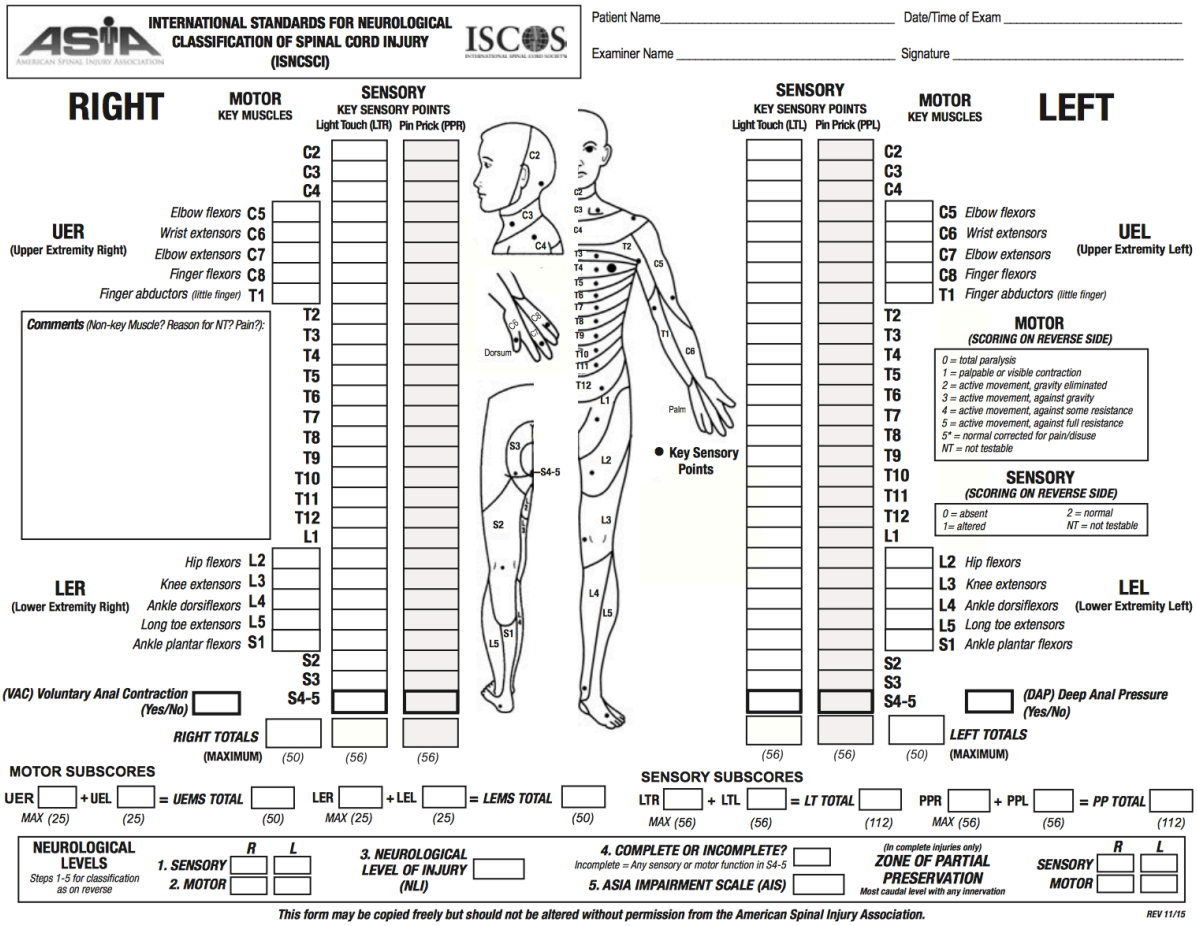
Abbreviations: AIS Conversion – improvement of at least 1 ASIA grade; CCI - Charlson Comorbidity Index; BMI – Body Mass Index; MVA – Motor vehicle accident; OHT – other high-energy trauma; ISS – Injury severity score; CCS – Central cord syndrome;

TABLE 4: AREA UNDER THE ROC CURVE (AUC) ANALYSIS TO PREDICT NEUROLOGICAL SEVERITY AND AIS CONVERSION

Group	Neurological Severity at 6 months	Neurological Severity at 1 year	AIS Conversion at 6 months	AIS Conversion at 1 year
MCC	0.33	0.33	0.28	0.28
MSCC	0.74	0.74	0.69	0.69
IML	0.96	0.96	0.93	0.93
BASIC	0.89	0.89	0.88	0.88
CASS	0.96	0.96	0.94	0.94

Abbreviations: ROC - Receiver Operating Characteristic; AUC – Area under the curve; AIS Conversion – improvement of at least 1 ASIA grade; MCC - Maximum canal compromise; MSCC - Maximum spinal cord compression; IML - Intramedullary lesion; BASIC - The Brain and Spinal Injury Center; CASS - Combined axial and sagittal score;

Appendix 1


INTERNATIONAL STANDARDS FOR NEUROLOGICAL CLASSIFICATION OF SPINAL CORD INJURY (ISNCSCI)
Patient Name
Date/Time of Exam
Examiner Name
Signature
RIGHT
MOTOR KEY MUSCLES
SENSORY KEY SENSORY POINTS
Light Touch (LTR)
Pin Prick (PPR)
UER (Upper Extremity Right)
Elbow flexors C5
Wrist extensors C6
Elbow extensors C7
Finger flexors C8
Finger abductors (little finger) T1
Comments (Non-key Muscle? Reason for NT? Pain?):
LER (Lower Extremity Right)
Hip flexors L2
Knee extensors L3
Ankle dorsiflexors L4
Long toe extensors L5
Ankle plantar flexors S1
(VAC) Voluntary Anal Contraction (Yes/No)
RIGHT TOTALS
(MAXIMUM)
Key Sensory Points
SENSORY KEY SENSORY POINTS
Light Touch (LTL)
Pin Prick (PPL)
MOTOR KEY MUSCLES
LEFT
C5 Elbow flexors
C6 Wrist extensors
C7 Elbow extensors
C8 Finger flexors
T1 Finger abductors (little finger)
UEL (Upper Extremity Left)
MOTOR (SCORING ON REVERSE SIDE)
0 = total paralysis
1 = palpable or visible contraction
2 = active movement, gravity eliminated
3 = active movement, against gravity
4 = active movement, against some resistance
5 = active movement, against full resistance
5* = normal corrected for pain/disuse
NT = not testable
SENSORY (SCORING ON REVERSE SIDE)
0 = absent
1= altered
2 = normal
NT = not testable
L2 Hip flexors
L3 Knee extensors
L4 Ankle dorsiflexors
L5 Long toe extensors
S1 Ankle plantar flexors
LEL (Lower Extremity Left)
(DAP) Deep Anal Pressure (Yes/No)
LEFT TOTALS
(MAXIMUM)
MOTOR SUBSCORES
UER + UEL = UEMS TOTAL
LER + LEL = LEMS TOTAL
SENSORY SUBSCORES
LTR + LTL = LT TOTAL
PPR + PPL = PP TOTAL
NEUROLOGICAL LEVELS
Steps 1-5 for classification as on reverse
1. SENSORY
2. MOTOR
3. NEUROLOGICAL LEVEL OF INJURY (NLI)
4. COMPLETE OR INCOMPLETE?
Incomplete = Any sensory or motor function in S4-5
5. ASIA IMPAIRMENT SCALE (AIS)
(In complete injuries only)
ZONE OF PARTIAL PRESERVATION
Most caudal level with any innervation
SENSORY
MOTOR
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REV 11/15